PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Mohsen Shahinpoor, Parsa Shahinpoor, & David Soltanpour	Art Unit: 1615
Serial No.	: 10/064,698	Examiner: Redford O Berko
Filed	: August 7, 2002	Docket No.: 2002-44-MO
For	: Nitric Oxide (NO) Donor+cGMP-PDE5 Inhibitor As A Topical Drug For Enhanced Hair Growth	

RESPONSE TO OFFICE ACTION

ATTN: COMMISSIONER FOR PATENTS
PO BOX 1450
ALEXANDRIA, VA 22313-1450

Sir:

This paper is in response to the office action dated November 17, 2004. Please amend the application, without prejudice, as follows:

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: ATTN: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on the ___11__day of ____February_____, 2005.

Mohsen Shahinpoor, Parsa Shahinpoor, David Soltanpour
Date Signed: February 11, 2005

Dear Examiner,

Please amend the claims as follow and consider our remarks:

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1- (Amended) Method for enhancing hair growth or diminishing hair loss or alopecia, in mammals, comprising administering topically to the skin a mixture of a nitric oxide (NO) donor such as minoxidil, or 6-(1-piperidinyl)pyrimidine-2,4-diamine 3-oxide and a cyclic guanosine 3',5'-monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) inhibitor such as sildenafil citrate ($C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$) in a dermatologically acceptable solution mix.

2- (Original) Method according to claim 1, wherein said topical dermatological compound is in the form of an aqueous solution or suspension, or in the form a gel, a shampoo, an ointment or a cream in a pharmaceutically acceptable dermatological vehicle or carrier to be applied to the mammalian skin.

3- (Amended) Method according to claim 1, wherein the Nitric Oxide (No) releasing agent in said dermatological mix is glyceryl trinitrate or nitroglycerine (C3H5N3O9)

4- (Amended) Method according to claim 1, wherein the Nitric Oxide (No) releasing agent in said dermatological mix is L-arginine or ($C_6H_{14}N_4O_2$).

5- (Amended) Method according to claim 1, wherein the Nitric Oxide (No) releasing agent in said dermatological mix is a isosorbide dinitrate or ($C_6H_8N_2O_8$)

6- (Amended) Method according to claim 1, wherein the Nitric Oxide (No) releasing agent in said dermatological mix is nitroprusside or (Na2Fe(CN)5NO.2H2O)

7- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is S-nitrosylated-proteins/peptides.

8- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is S-nitrosylated oligosaccharides and polysaccharides.

9- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is a Nonoate compounds such as piperazines 2 and diazeniumdiolates.

10- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is an inorganic nitroso compound such as sodium nitroprusside.

11- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is Sydnonimines.

12-(Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is L-arginine (which does not release NO directly, but rather is an enzyme substrate which leads to the formation of nitric oxide in vivo).

13- (Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is 1,3-(nitrooxymethyl)phenyl 2-hydroxybenzoate isosorbide dinitrate.

14-(Withdrawn) Method according to claim 1, wherein the No releasing agent in said dermatological mix is pyrimidine (also known as Minoxidil or Rogaine.sup.RTM).

15- (Withdrawn) Method according to claim 1, wherein the cGMP specific PDE-5 inhibitor in said dermatological mix is (sildenafil) also known as 1-[[3-(6,7dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-y- l)-4 ethoxyphenyl]sulphonyl]-4-methylpiperazine.

16- (Withdrawn) Method according to claim 1, wherein the cGMP specific PDE-5 inhibitor in said dermatological mix is sildenafil citrate, (Viagra.sup.RTM) also known as 1-[[3-(6,7dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyri- midin-5-yl)-4 ethoxyphenyl]sulphonyl]-4-methylpiperazine citrate.

17- (withdrawn) Method according to claim 1, wherein the cGMP specific PDE-5 inhibitor in said dermatological mix is 3-ethyl-5-[5-(4-ethylpiperazin-1-ylsulphony- l)-2-n-propoxyphenyl]-2-(pyridin-2yl)methyl-2,6-dihydro-7H-pyrazolo[4,3-d]- pyrimidin-7-one.

18- (Withdrawn) Method according to claim 1, wherein the cGMP specific PDE-5 inhibitor in said dermatological mix is 1-{6-ethoxy-5-[3-ethyl-6,7-dihydro-2-(2-met- hoxyethyl)-7-oxo-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-3 pyridylsulphonyl}-4-ethylpip-erazine.

19- (withdrawn) Method according to claim 1, wherein said topical dermatological mix is in the form of an aqueous solution and further contains one or more tonicity adjusting agents, one or more buffers and one or more antioxidants.

20- (Withdrawn) Method according to claim 1, wherein said topical dermatological mix further contains one or more antimicrobial agents.

21- (Original) The composition according to claim 1, wherein said dose is in pill form for oral administration.

22- (Original) The method according to claim 1, wherein said topical dermatological mix further contains one or more combinations of NO donors and cGMP PDE5 inhibitors.

23- (Original) The method according to claim 1, wherein said topical dermatological mix further contains one or more weight or volume percentage combinations of NO donors and cGMP PDE5 inhibitors.

24- (Withdrawn) A composition according to claim 1 wherein said composition also includes a pharmaceutically effective vehicle for said compound.

25- (Original) A composition according to claim 1 used in veterinary preparations or feeds to increase the rate of growth of fur (pelt) in certain fur bearing animals and to retard shedding and molting.

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Thus the new set of claims is:

1- Method for enhancing hair growth or diminishing hair loss or alopecia, in mammals, comprising administering topically to the skin a mixture of a nitric oxide (NO) donor such as minoxidil, or 6-(1-piperidinyl)pyrimidine-2,4-diamine 3-oxide and a cyclic guanosine 3',5'-monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) inhibitor such as sildenafil citrate ($C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$) in a dermatologically acceptable solution mix.

2- Method according to claim 1, wherein said topical dermatological compound is in the form of an aqueous solution or suspension, or in the form a gel, a shampoo, an ointment or a cream in a pharmaceutically acceptable dermatological vehicle or carrier

to be applied to the mammalian skin.

3- Method according to claim 1, wherein the No releasing agent in said dermatological mix is glyceryl trinitrate or nitroglycerine (C3H5N3O9)

4- Method according to claim 1, wherein the No releasing agent in said dermatological mix is L-arginine or ($C_6H_{14}N_4O_2$).

5- Method according to claim 1, wherein the No releasing agent in said dermatological mix is a isosorbide dinitrate or ($C_6H_8N_2O_8$)

6- Method according to claim 1, wherein the No releasing agent in said dermatological mix is nitroprusside or (Na2Fe(CN)5NO.2H2O)

7-The composition according to claim 1, wherein said dose is in pill form for oral administration.

8-The method according to claim 1, wherein said topical dermatological mix further contains one or more combinations of NO donors and cGMP PDE5 inhibitors.

9-The method according to claim 1, wherein said topical dermatological mix further contains one or more weight or volume percentage combinations of NO donors and cGMP PDE5 inhibitors.

10- A composition according to claim 1 used in veterinary preparations or feeds to increase the rate of growth of fur (pelt) in certain fur bearing animals and to retard shedding and molting.

These claims have been revised and amended or withdrawn based on the Examiners' election/restrictions under 35 USC 103, 35 USC 112.

Please consider the following remarks in support of the revised claims and in connection with rejections under 35 USC 103:

REMARKS

Response to Claim Rejections under 35 USC 103:

The essential reason for rejection of basic claims 1, 3, 4, 5, 9, 10-19 by the Examiner is that the combination of Nitric Oxide (No) donors and cGMP-PDE5 inhibitors to enhance hair growth and or diminishing hair loss or alopecia was obvious to one of ordinary skill in the art by 2002 (Wallace, 6, 476, 037), because Green et al (5,358, 714) in 1994 and Garfield et al (5, 698,738) in 1997 teaches Nitric Oxide (No) donors as having the ability to improve hair growth and in 2002, Wallace (6, 476, 037) teaches the synergistic effect of Nitric Oxide (No) donors like L-Arginine and Phosphodiestrase Inhibitors such as Sildenafil in the treatment of cardiac pathologies and/or the treatment of erectile

dysfunction (abstract). We humbly beg the Examiner to consider the facts that Wallace was skilled in the art and he did see the synergistic effect of L-Arginine and PDE and he did extend his claims to cover two distinctly different medical areas such as cardiovascular and erectile dysfunction but did not claim synergistic enhancement of hair growth in some 44 claims that he stated. We humbly maintain that this was not an obvious claim for him, otherwise he would have stated it, as also the Examiner has noted on page 3, paragraph 1 of the office action. Furthermore, we maintain that cGMP-PDE-5 inhibitors such as sildenafil citrate (which is the acidic salt of Sildenafil) or sildenafil itself do not enhance hair growth, as stated by the Examiner in the 4th. Paragraph on page 3 of the office action. We humbly maintain that all cGMP-PDE5 inhibitors do is to inhibit the formation of cGMP specific enzyme PDE-5 that destroys cGMP, which is the vasodilator enzyme, created by Nitric Oxide (NO) donors. If no cGMP is present, which means no Nitric Oxide (NO) donor is present, then Sildenafil Citrate by itself cannot do vasodilation and thus cannot affect hair growth. However, our disclosure combines Nitric Oxide (NO) donors with cGMP-PDE5 inhibitors to enhance the effect of Nitric Oxide (NO) donors as hair growth medicine. Please refer to our sections 0009-0012 amongst others for detailed discussions on these issues. To simply argue it, cGMP-PDE5 does not by itself enhance hair growth and is not a microvasodilator agent. All it does is that it inhibits the formation of enzyme PDE5 that specifically destroys enzyme cGMP, which is a microvasodilator, produced by Nitric Oxide (NO) donors. These are fully explained in our disclosure and in particular sections 0009-0012. This synergistic combination was not obvious to Wallace (037), as the Examiner has also noted. The reason why cGMP-PDE5 in the form of Viagra works as erectile enhancer (vasodilation of pennies) is not because it does vasodilation for erection and enhanced blood flow to the penis, but because it slows down the destruction of cGMP enzyme produced naturally by the body when arousal occurs by the enzyme PDE5 produced by the body to suppress it. In individuals with hair growth or alopecia problems no such natural production of cGMP in the hair follicle or skin with hair is documented and thus using cGMP-PDE5 inhibitor such as Sildenafil Citrate (Viagra) or its pure chemical Sildenafil for hair growth will not work by itself and there is no published document proving that. We respectfully ask the Examiner to consider our intricate medical points in this discussion and do not consider the Nitric-Oxide (NO) donor+cGMP-PDE5 combination as an obvious issue for hair growth because Wallace in his 44 claims on vastly different areas of medical treatment did not see the enhancing effect of the combination of NO donors and cGMP-PDE5 inhibitor on hair growth, as the Examiner has also noted.

On the 35 USC 103 rejection of our claims 1, 6, 7, 8 and 20-25 on the basis of Wallace (037) in view of Rogers et al (6, 747, 008) and Buzzano (5, 183, 817) and Buzzano et al (5, 514, 672) we have the following comments in addition to the fundamental comments made above:

Rogers (008) has not disclosed that combination of Nitric Oxide (NO) donors and cGMP-PDE5 inhibitors, as the Examiner also has noted. Not only this hair growth enhancement or prevention of alopecia was not obvious to Wallace (037), it was certainly not obvious to Rogers (008) either. Regarding Buzzano (817) and Buzzano et

al (672) please note that they combine a Nitric Oxide (NO) donor such as Minoxidil with Retinoids, which are shown to cause elevated DNA synthesis in keratinocytes in cell culture and thus has nothing to do with cGMP-PDE5 inhibitors which inhibit the formation of PDE5. True that they propose the idea of enhancing the effect of Minoxidil by the addition of Retinoids but our enhancement is by the addition of cGMP-PDE5 inhibitors, which operate entirely differently from Retinoids.

We have also eliminated all trademark references in our revised set of claims to address the Examiners objection.

Having responded to each and every objection and rejection raised by the Examiner, it is believed that the patent application is now in condition for allowance, and such allowance is respectfully requested. If the Examiner has any questions or suggestions for expediting an allowance in this matter, the Examiner is invited to call the undersigned collect.

The Commissioner is authorized to charge any required fees, which may be required during the entire pendency of the application.

Respectfully submitted,

Dated: February 11, 2005

By: _____

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